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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,394	05/03/2000	THOMAS CARLSSON	45687-00008	5034

7590 09/03/2003

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EXAMINER

GAKH, YELENA G

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 09/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/462,394

Applicant(s)

CARLSSON, THOMAS

Examiner

Yelena G. Gakh, Ph.D.

Art Unit

1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 May 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 12-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 May 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-11, drawn to a method of regenerating a biosensor.

Group II, claim(s) 12-18, drawn to a system for continuous monitoring of analytes.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Group II lack special technical feature, since the system recited in claim 12 is disclosed in the prior art, e.g. Ligler et al. (US 5,183,740), which discloses a system for continuous monitoring analytes in a biological fluid, comprising a biosensor with the fluid passage, means for passing a flow of a background fluid at selectable flow rates and a means for increasing such flow rate, along with means for providing a signal for a signal generating portion, and a sampling device (Abstract, Figure). Therefore, the inventions of Groups I and II do not share a special technical feature and the restriction is valid.

2. During a telephone conversation with Lekha Gopalakrishnan on 08/27/03 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-11. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

3. The disclosure is objected to because of the following informalities: on page 10, lines 24 and 27 "increaseded" is a misspelled word. Appropriate correction is required.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. **Claims 1-11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Luong et al. (US 5,411,866).

Luong teaches a method of determining bioactive substances in biological fluids, including blood, with biosensors, wherein analytes, such as glutamine, are detected in the presence of interfering compounds, e.g. glutamate; the method comprising a step of regenerating biosensor by washing. Luong teaches, "the signals did not return to the normal zero baseline during the washing step implying a slow dissociation of bound glutamate from the resin. As expected, the sample stream flow rate also affected the glutamate binding capacity of the acetate resin column. Below 40 ml/h less than 1% of the injection of glutamate passed through the resin, whereas at 100 ml/h this value increased up to 5%" (col. 8, lines 56-64). "As a compromise

Art Unit: 1743

between sensitivity of analysis and sample throughput (assays per hour) a flow rate of 31 ml/h [0.5 ml/min] was selected for all subsequent studies. It should be noted that the total flow rate through the immobilized enzyme column will be 62 ml/h [1 ml/min] after the two streams merge" (col. 8, lines 7-13).

It would have been obvious for anyone of ordinary skill in the art to increase the washing buffer flow after detecting the analyte in order to return the baseline to zero by increasing dissociation of glutamate from the resin, because Luong emphasizes that slow dissociation of interfering glutamate leads to a non-zero baseline and that increased buffer flow increases dissociation of glutamate.

It would have been obvious for anyone of ordinary skill in the art to establish such zero baseline by passing the buffer flow without the analyte through the biosensor, because this is a conventional calibration step in analytical practice. It would have been obvious to continue washing with increased rate of the buffer flow until the baseline reaches zero (a predetermined value).

It would have been obvious for anyone of ordinary skill in the art to optimize conditions of detection and regeneration by optimizing the speed of the buffer flow and the time of washing, depending on the system analyzed, see *In re Boesch*, 205 USPQ 215 (CCPA 1980): the discovery of an optimum value of a known result effective variable without producing any new or unexpected results is within the skill of the routineer in the art.

It would have been obvious for anyone of ordinary skill in the art to dispose the sample, which is not analyzed, as waste, because this is the only possible way of disposing a material in a conventional mode of analysis when the samples are periodically withdrawn for analysis from a continuous flow.

It would have been obvious for anyone of ordinary skill in the art to use anticoagulant, specifically in 1:1 ratio with the blood sample, because this is a standard practice for blood analyses as mentioned by the Applicant.

7. **Claims 1-11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Edelmann et al. (US 4,153,513, IDS) in view of Wong (US 5,165,406).

Edelmann teaches a method "for the continuous determination of the concentration of an enzyme substrate" (Title) in a blood sample, comprising "an intermittent introduction in which

Art Unit: 1743

the volumes of sample move block-like in the current of buffer solution” (col. 3, lines 40-50) with pure buffer solution flowing through the detector between the measurements.

Anticoagulant is mixed with the blood sample in 1:1 ratio (5 ml/hr of heparin solution and 5 ml/hr of blood, col. 6, lines 53-56), the measurements are performed every 30 sec (col. 4, lines 56-60).

Edelmann does not specifically disclose regenerating the biosensor by increasing the flow rate of the buffer after detecting the analyte.

Wong discloses an electrochemical biosensor apparatus for detecting blood analytes and a method of its regeneration comprising washing step between the measurements, which involves turbulent agitating flow of infusion or calibration liquid “that helps dislodge any blood cells collected around the electrodes, as well as other parts of the assembly. This reduces the collection of blood cells, increases the measurement accuracy, and reduces the purge volume necessary for accurate measurement, thereby reducing the time interval between successive measurements” (col. 3, lines 37-46).

Although Wong does not specifically indicate increasing the flow rate of the washing buffer between measurements (i.e. after the signal is detected and until the zero background is achieved), turbulent flow has the same effect as increased rate of a laminar flow; therefore it would have been obvious for anyone of ordinary skill in the art to modify Edelmann’s method by simply increasing the flow rate of the washing buffer between measurements instead of using specially designed helical groove for creating turbulent flow disclosed by Wong, because such increase of the flow rate has the same effect of more efficient cleaning the sensor, as Wong’s turbulent flow. It would have been obvious for anyone of ordinary skill in the art to optimize this rate to make it higher than the rate of the analyte flow (10 ml/hr).

Conclusion

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. *Hayashi et al. (US 5,306,4123)* discloses assay apparatus and method, comprising providing a buffer flow rate of about 1.0 ml/min (col. 9, lines 1-2); *Hogan et al. (US 5,449,064)* discloses “on-line interface and valve for capillary electrophoresis system” with merely buffer

Art Unit: 1743

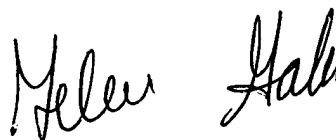
solution flowing from the inlet tube "during the time between sample of analyte" (col. 13, lines 55-64); *Schneider et al. (US 5,861,254)* discloses a "flow cell SELEX" which allows varying the flow rate of the sample and buffer.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (703) 306-5906. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

Yelena Gakh
8/28/03

A handwritten signature in black ink, appearing to read "Yelena Gakh", is written over the typed name and date.